

CASE REPORT

Clear-cell sarcoma of the small intestine detected by FDG-PET/CT during comprehensive examination of an inflammatory reaction

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Abstract : Clear-cell sarcoma (CCS) is a rare, malignant, soft-tissue tumor, which involves the extremities, particularly the foot and foot joint tendons and aponeuroses. It is morphologically similar to but histochemically distinct from malignant melanoma. CCS arising in the gastrointestinal tract has rarely been reported. The prognosis of CCS is reportedly poor because of the high incidence of metastases at the time of initial diagnosis and the high frequency of recurrence. We report a case of early-stage CCS of the small intestine detected by ¹⁸F-fluoro-2-deoxy D-glucose Positron Emission Tomography/Computed Tomography (FDG-PET/CT) during the comprehensive examination of an inflammatory reaction. In this case, FDG-PET/CT clearly visualized the lesion, which was difficult to detect by contrast CT. *J. Med. Invest.* 56 : 70-75, February, 2009

Keywords : clear-cell sarcoma, gastrointestinal tract, FDG-PET/CT, malignant melanoma

INTRODUCTION

Clear cell sarcoma (CCS), also known as melanoma of soft parts, typically presents in the deep soft tissues of the lower extremity, in close proximity to tendons, fascias, or aponeuroses. Young adults are preferentially affected and the clinical course is often marked by regional and distant metastases with a reported 5-year survival rate of 50-60%. Most CCS show immunoreactivity for melanoma markers, such as HMB45, and contain melanosomes. Indeed, most CCS share a melanocytic gene expression signature with melanomas. However, CCS are also genetically distinct from melanomas, as they lack BRAF

mutations and show, in most cases, a recurrent chromosomal translocation t(12 ; 22)(q13 ; q12), resulting in the fusion of EWS gene on 22q12 with the activating transcription factor-1 gene (ATF1) on 12q13 (1, 5).

Primary CCSs of the gastrointestinal tract are rare. Gastrointestinal CCS includes a histologic variant rich in osteoclast-type giant cells which uniformly express S100 protein. As a result of its rarity in the gastrointestinal tract, the differential diagnosis of CCS in this site includes more common mesenchymal or neuroectodermal neoplasms, such as gastrointestinal stromal tumors, Schwannoma, carcinoid, or metastatic melanoma (1-4).

We report a case of early-stage Clear cell sarcoma (CCS) of the small intestine detected by ¹⁸F-fluoro-2-deoxy D-glucose Positron Emission Tomography/Computed Tomography (FDG-PET/CT) during comprehensive examination of an inflammatory reaction.

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CASE REPORT

The patient was a nursing student in her early twenties with no particular chief complaint. During practical training, she noted that her erythrocyte sedimentation rate (ESR) was elevated, and visited the Department of Internal Medicine of our hospital one month later. At the first examination, her C-reactive protein (CRP) was 3.7 mg/dl (normal < 0.3 mg/dl), and ESR 80 mm/h (normal range, 3-15 mm/h). For the differential diagnosis of infection, collagen disease and malignant tumor, plain chest CT and a planar gallium whole-body scan were performed, but no causative lesions were identified. During subsequent follow-up, her inflammatory reaction persisted (CRP 6-9 mg/dl, ESR 100-130 mm/h). Nine months after the first examination at the Department of Internal Medicine at our hospital, she developed common cold symptoms and a low-grade fever, and showed a persistently high CRP; therefore, she was admitted to the same department for further evaluation.

On admission, her temperature was 37.6°C, blood pressure 120/80 mmHg, and pulse 84 bpm and regular. The palpebral conjunctivae were anemic. The throat was not red. No cervical lymphadenopathy was noted. The heart and breath sounds were normal. The abdomen was flat and soft, with no tenderness. No edema or joint pain was present. She experienced no weight loss. No motor or sensory deficit was identified.

On admission, blood tests showed microcytic anemia, thrombocytosis and elevated CRP (15.5 mg/dl) which meant chronic inflammatory reaction. However rheumatoid factor (RF) was slightly elevated, and antinuclear antibody was positive, it was difficult to determine the cause on inflammatory reaction collagen disease. Contrast CT of the chest, abdomen and pelvic region was performed, which suggested small lymph node lesions around the pelvic arteries (Fig. 1). Although the small intestinal lesion existed at that time, we could not detect it. The patient did not have much fat in the abdominal cavity, therefore, the organs were in close proximity to each other, and the small intestinal lesion was enhanced similar to the normal intestine. Therefore, it was difficult to detect the lesion only by contrast CT.

The mild common cold symptoms noted on admission suggested the presence of infection, but antibiotic administration did not improve the low-grade fever or CRP level. To exclude blood disorders, bone marrow aspiration was performed, but no



Fig. 1. (a) Upon admission, contrast CT suggested lymph node enlargement around the arteries anterior to the sacral bone (arrow). (b) Arrow indicates the neoplastic lesion that was difficult to detect upon admission.

abnormalities were found. The inflammatory reaction had increased for about 1 year, but various examinations revealed no abnormalities we could detect. Thus, to search for infectious foci and neoplastic disease again, we performed FDG-PET/CT.

FDG-PET showed an abnormal, mass-like uptake (*Standardized Uptake Value (SUV)max 10) on the right side of the pelvic cavity and another nodular uptake (SUVmax 3.3) anterior to the sacral bone (Fig. 2). The abnormal uptake in the right pelvic cavity corresponded on CT to a structure that consisted of soft-tissue-density areas mixed with low-density areas (Fig. 3). The presacral uptake corresponded to soft-tissue densities on CT (Fig. 4). A second look at the admission CT scans in comparison with the abnormal uptake in the right pelvic cavity on FDG-PET showed a solid, contrast-enhanced, mass-like structure in the intestinal lumen or wall, at about the same level (Fig. 1a). The presacral uptake corresponded on CT to soft-tissue densities that apparently surrounded the blood vessels, which suggested soft-tissue tumors including malignant lymphoma (Fig. 1b). However, the SUVmax of 3.3 was not high enough to confidently diagnose malignancy. The presacral uptake might be reactive lymph nodes caused by long-term inflammatory

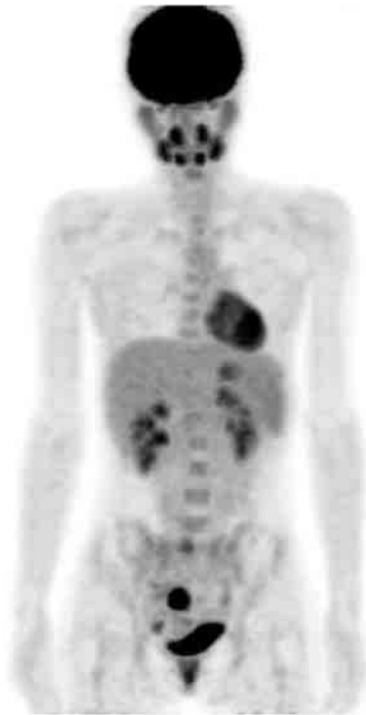


Fig. 2. FDG-PET maximum intensity projection (MIP) images showed a strong, mass-like uptake on the right side of the pelvic cavity and a nodular uptake anterior to the sacral bone. Low-level uptake in the right pelvic cavity corresponded to the ovary on CT.

reaction.

Barium contrast radiography of the small intestine revealed an approximately 2.5 cm submucosal mass

with a surface depression and good passage of barium through this region (Fig. 5).

Laparoscopic, segmental small-intestine resection was performed about 1 month after admission. During surgery, a 4 cm tumor was found about 150 cm proximal to the end of the ileum. In addition to the presacral lymph nodes observed on FDG-PET/CT, many of the mesenteric lymph nodes were enlarged. Some of these nodes were submitted for frozen section diagnosis, but no malignant lesions were found. Frozen section examination of the small intestinal tumor suggested malignant lymphoma. Based on these findings, some of the lymph nodes with FDG uptake were collected, and small intestinal resection was performed.

The resected specimen contained a 3 cm tumor with a surface ulcer that corresponded to the depression on Barium contrast radiography of the small intestine. On the cut surface, the tumor involved the muscular layer, but left the serosa intact (Fig. 6). Histopathological examination revealed a submucosal, nodular lesion composed of short, spindle-shaped cells with clear cytoplasm. As many as 7-9 mitotic figures per high-power field (magnification $\times 400$) were seen, which suggested malignancy (Fig. 7b). Osteoclast-like, multinucleated giant cells were present among tumor cells (Fig. 7a). Since the origin of the tumor could not be identified by H-E staining alone, immunostaining was performed. As

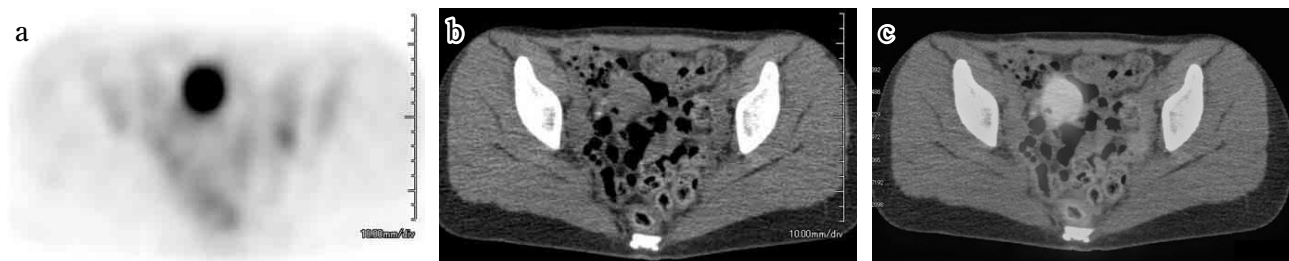


Fig. 3. (a) FDG-PET revealed abnormal uptake (SUVmax 10) in the right pelvic cavity. (b) Uptake corresponded on CT to a structure that consisted of soft-tissue-density areas mixed with low-density areas, which suggested a small intestinal lesion. (c) FDG-PET/CT image resulting from (a) superimposed on (b).



Fig. 4. (a) FDG-PET showed uptake (SUVmax 3.3) anterior to the sacral bone. (b) Uptake corresponded to soft-tissue density on CT. (c) FDG-PET/CT image resulting from (a) superimposed on (b).

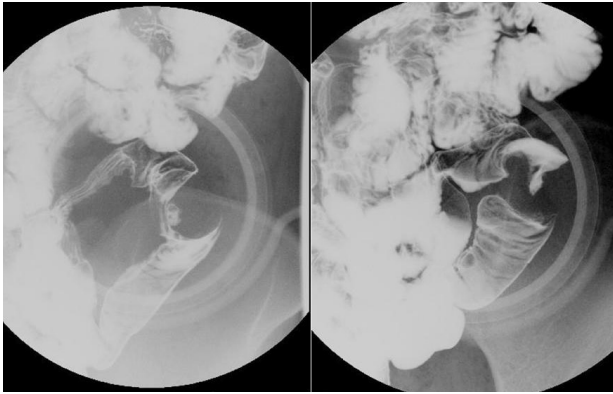


Fig. 5. Small intestinal fluoroscopy revealed an 2.5 cm submucosal mass with a surface depression in the ileum.

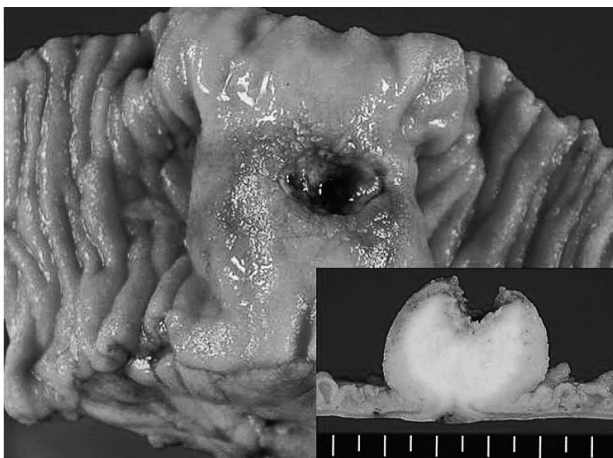


Fig. 6. The resected specimen contained a 3 cm tumor with a surface ulcer. On the cut surface, the tumor involved the muscular coat, but left the serosa intact.

a result, the tumor cells were positive for S-100 protein (Fig. 8a). Reverse Transcriptase-Polymerase Chain Reaction (RT-PCR) was performed, suggesting a translocation resulting in EWS-ATF1 gene fusion (Fig. 8b).

These findings led to the diagnosis of CCS. No malignant features were observed in the surgically resected lymph nodes with increased FDG uptake, as detected by FDG-PET/CT.

FDG-PET/CT, performed 3 months after surgery, revealed no abnormal uptake suggestive of metastasis or recurrence (Fig. 9). The presacral lymph nodes, which had exhibited abnormal uptake before surgery, were reduced in size, and showed no detectable uptake, which suggested that the pre-operative uptake was due to inflammation (Fig. 10). After surgery, the ESR and CRP returned to normal. Currently, 2 years after surgery, the patient is free from recurrence and metastasis.

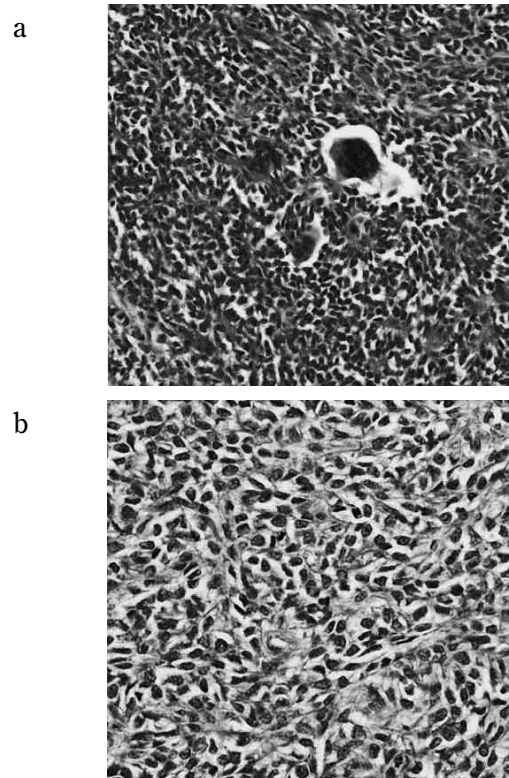


Fig. 7. (a) Histopathological image of the tumor at low magnification ($\times 100$). Osteoclast-like, multinucleated giant cells were present among tumor cells. (b) At high magnification ($\times 400$), a submucosal, nodular lesion composed of short, spindle-shaped cells with clear cytoplasm was observed.

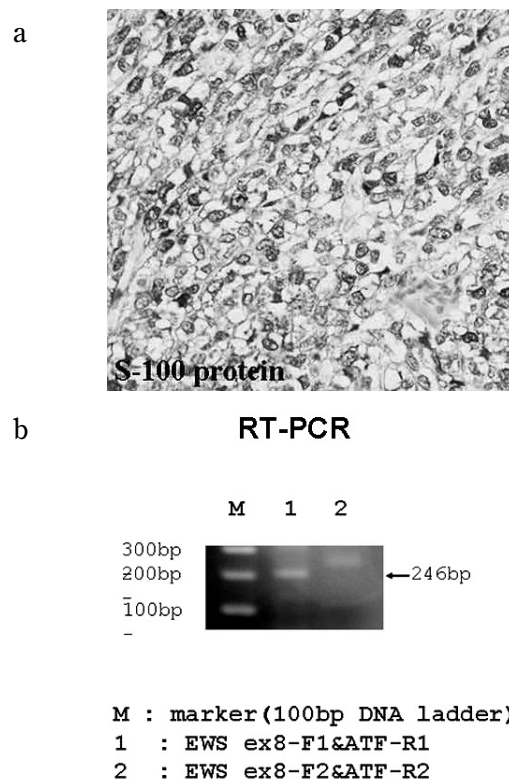


Fig. 8. (a) Histopathological immunostaining view at high magnification ($\times 400$). The tumor cells were positive for S-100 protein. (b) RT-PCR showed EWS-ATF1 fusion gene.

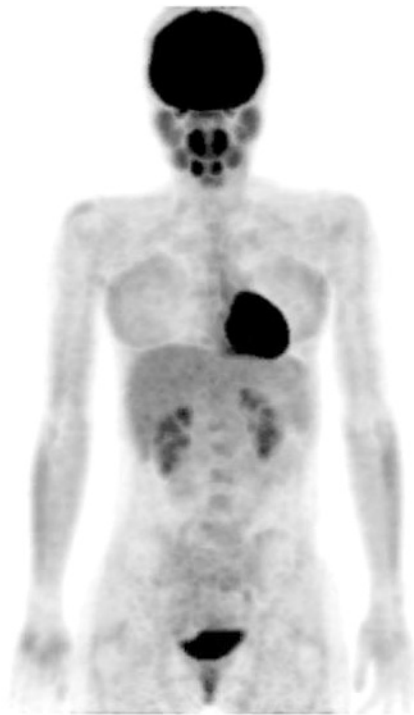


Fig. 9. FDG-PET MIP image obtained 3 months after surgery. No abnormal uptake suggestive of metastasis or recurrence was observed.

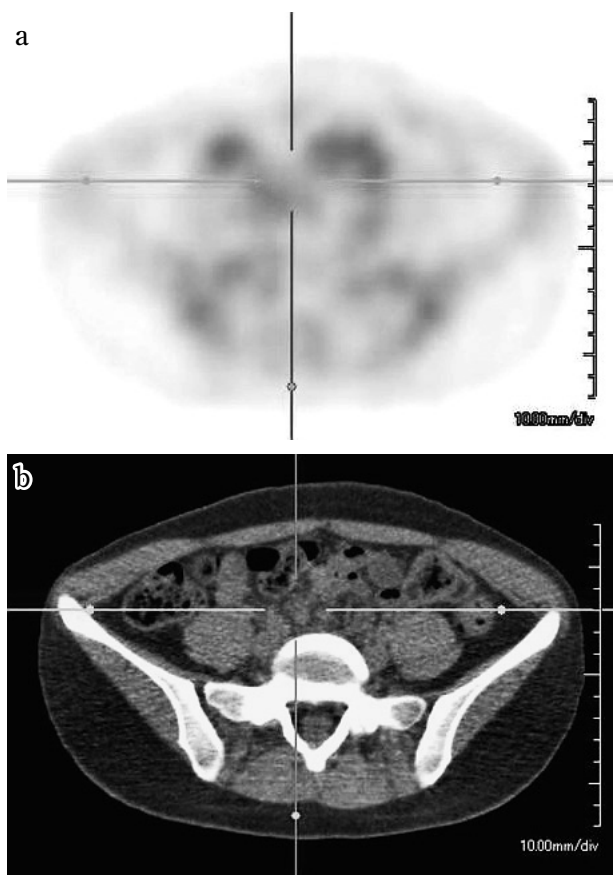


Fig. 10. Axial view images of FDG PET/CT after 3 months after surgery. (a) Presacral lymph nodes, which had exhibited abnormal uptake before surgery, showed no detectable uptake. (b) Upon CT, the presacral lymph nodes were reduced in size.

DISCUSSION

The incidence of CCS of gastrointestinal tract origin is much lower, in the small intestine, large intestine and stomach, in decreasing order of frequency. The tumor grows transmurally, and is reportedly often associated with ulceration and lymph node metastasis. Molecular detection of the EWS/AFT1 fusion gene establishes the diagnosis (1-4). Comin, *et al.* (5) reported 16 patients who were diagnosed with gastrointestinal CCS. Their mean age was 39 years, and the tumor was found frequently in women, mostly in the small intestine, had a mean diameter of 3 cm, and was frequently associated with ulceration and full-thickness invasion. In many patients, CCS starts with disturbed passage of stools and weight loss, but laboratory tests, including blood tests, reveal no abnormalities in some patients. Local lymph node metastasis or mesenteric dissemination is observed in about half of the patients at the time of diagnosis, and liver metastasis, peritoneal dissemination, pancreatic metastasis, or lung metastasis in most patients. The present CCS arose in the small intestine of a young woman, similar to previously reported cases, but the lesion was localized in the small intestine, with no metastasis, as demonstrated by biopsies of the enlarged lymph nodes. In this case, a planar gallium whole-body scan was negative at the first examination. Contrast CT of the chest, abdomen and pelvic region performed after 1 year, but it was difficult to detect the small intestinal lesion. The patient did not have much fat in the abdominal cavity, therefore all the organs were in close proximity to each other, and the lesion was enhanced similarly to normal intestine. To establish the reason for the increased inflammatory reaction, we performed FDG-PET/CT, which revealed obvious abnormal uptake. Neither FDG-PET/CT nor contrast CT contributed to the diagnosis, but FDG-PET/CT was useful for detecting the lesion. Hereafter, FDG-PET/CT might help to detect the small intestinal lesion such as gastrointestinal stromal tumors, carcinoid, or metastatic melanoma, which is difficult to distinguish from normal intestine as our case. Besides, FDG-PET/CT might be helpful in detecting postoperative recurrence of CCS of gastrointestinal origin. Our literature search revealed reports of the usefulness of FDG-PET/CT in the detection of postoperative recurrence of CCS that developed in the soft tissue of bone (6), but no detection of CCS of gastrointestinal origin.

In conclusion, we report a patient with small intestinal CCS that was detected by FDG-PET/CT. Gastrointestinal CCS is a very rare, malignant tumor that is often advanced at the time of diagnosis. In this patient, FDG-PET/CT, performed during comprehensive examination of a prolonged inflammatory reaction, clearly visualized the lesion, which was difficult to detect by other imaging techniques, and therefore had a marked clinical impact.

*Supplementary explanation of standardized uptake value (SUV).

$SUV = \text{tissue concentration (KBq/ml)} / \text{injected FDG dose (KBq)} / \text{body weight (g)}$

A popular usage of SUVs is their capability in helping to distinguish between benign and malignant lesions. For example, a study might find an SUV of 2.5 as appropriate for separating certain benign and malignant lesions. Caution, however, must be exercised using such a cutoff outside of the institution and the application for which it was determined (7).

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